

JMH Extended Infusion
Piperacillin/Tazobactam
Protocol

Why?
Optimize treatment efficacy with comparable or better clinical outcomes
Lower daily dose required
Fewer administration requirements
Cost Savings

Who?
Implementation house-wide
All Adult Inpatients

What?
No changes in prescribing patterns
Automatic conversion protocol
*****INFUSION TIME CHANGE****
Over 4 hours

When?
Implementation: October 5, 2010
Quality Assurance Audit
October 5-31, 2010
Evaluating administration technique and identifying areas for improvement

Dosage conversion between intermittent and extended infusion regimens

Creatinine Clearance	Intermittent Dosing	Extended Infusion Dosing
> 20 mL/min or CVVHD	4.5 gm IV q6h*	4.5 gm IV q6h (3hr)
	All Other Regimens	3.375 gm IV q8h (4hr)
< 20 mL/min or HD	All Regimens	3.375 gm IV q12h (4hr)

*4.5 gm IV q6h (3hr) reserved for patients with pneumonia caused by *Pseudomonas aeruginosa* or as an empiric regimen in the intensive care units

**Jackson Memorial Hospital
EXTENDED INFUSION PIPERACILLIN/TAZOBACTAM (ZOSYN®) PROTOCOL**

Background

- Piperacillin/tazobactam is often used for empiric coverage and treatment of gram negative infections
 - Exhibits time-dependent activity
 - Time above the minimum inhibitory concentration (MIC) for penicillins needed to achieve adequate antimicrobial activity is greater than or equal to 50% of the dosing interval
- Three dosing strategies have been studied:
 - Intermittent infusion (infused over 30 minutes)
 - Traditional dosing strategy
 - Maintains sufficient plasma levels for activity while occupying the line for a minimal amount of time throughout the day
 - Recent concerns developed with ability to maintain sufficient plasma levels with the emergence of increasing MIC values among organisms, in particular *Pseudomonas aeruginosa*
 - Daily dose generally 3.375 grams IV q6h over 30 minutes
 - **Extended infusion (infused over 4 hours)**
 - Plasma levels maintained above the MIC more consistently as compared to intermittent
 - Requires extended time of line use, however provides sufficient line-free intervals for infusion of other medications
 - With more consistent levels above MIC, the daily dosage requirements are reduced, providing an economic advantage
 - Studies have shown no increased risk of mortality or length of stay in patients with *Pseudomonas aeruginosa* or other gram negative infections treated with extended infusion regimens as compared to intermittent infusion regimens
 - Daily dose generally 3.375 grams IV q8h over 4 hours
 - Continuous infusion
 - Constant plasma levels
 - Concerns with drug interactions and access requirements
 - Daily dose generally 13.5 grams over 24 hours

Jackson Memorial Hospital Antibigram – January to June 2010

- In an effort to maintain current standards of practice in congruence with evidence based medicine and JMH formulary policies, cefepime will continue to be advocated as the agent of choice for empiric coverage and treatment of *Pseudomonas aeruginosa* infections.
- This is due to the fact that cefepime continues to exhibit a better susceptibility profile for *P. aeruginosa* than piperacillin/tazobactam for Jackson Main hospital using the more conservative susceptibility breakpoint of 16 mcg/mL implemented at JMH (Figure 1).

Figure 1: Jackson Memorial Hospital Antibigram: P. Aeruginosa isolates from January to June 2010

GRAM-NEGATIVE ISOLATES	No.	Percent susceptible													
		AM	AMC	TZP	CZ	FOX	CRO	FEP	ERT	IMP	AN	GM	TOB	LVX	SXT
<i>Pseudomonas aeruginosa</i>	623	/	/	71	/	/	/	83	/	86	94	80	92	63	/

Pip/tazo: 71% vs. Cefepime 83% susceptibility

Protocol Proposal/Implementation

- (Please see algorithm on reverse side)

Education

- **Physician staff** – No changes in prescribing patterns are required. Orders will be converted from intermittent to extended infusion as per protocol by clinical practice pharmacy staff
- **Nursing staff** – All Pip/Tazo orders received post-implementation date must be administered based on dosage conversion table provided in algorithm
 - MUST be infused over extended period
 - Time of infusion will be specified on the label from pharmacy
 - 4 hours for 3.375 gm doses
 - 3 hours for 4.5 gm doses

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Protocol approved by JMH P&T in September 2010